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Original Contribution

Does Smoking Reduction in Midlife Reduce Mortality Risk? Results of 2 Long-Term Prospective Cohort Studies of Men and Women in Scotland

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A long-term cohort study of working men in Israel found that smokers who reduced their cigarette consumption had lower subsequent mortality rates than those who did not. We conducted comparable analyses in 2 populations of smokers in Scotland. The Collaborative Study included 1,524 men and women aged 40–65 years in a working population who were screened twice, in 1970–1973 and 1977. The Renfrew/Paisley Study included 3,730 men and women aged 45–64 years in a general population who were screened twice, in 1972–1976 and 1977–1979. Both groups were followed up through 2010. Subjects were categorized by smoking intensity at each screening as smoking 0, 1–10, 11–20, or ≥21 cigarettes per day. At the second screening, subjects were categorized as having increased, maintained, or reduced their smoking intensity or as having quit smoking between the first and second screenings. There was no evidence of lower mortality in all reducers compared with maintainers. Multivariate adjusted hazard ratios of mortality were 0.91 (95% confidence interval (CI): 0.75, 1.10) in the Collaborative Study and 1.08 (95% CI: 0.97, 1.20) in the Renfrew/Paisley Study. There was clear evidence of lower mortality among quitters in both the Collaborative Study (hazard ratio = 0.66, 95% CI: 0.56, 0.78) and the Renfrew/Paisley Study (hazard ratio = 0.75, 95% CI: 0.67, 0.84). In the Collaborative Study only, we observed lower mortality similar to that of quitters among heavy smokers (≥21 cigarettes/day) who reduced their smoking intensity. These inconclusive results support the view that reducing cigarette consumption should not be promoted as a means of reducing mortality, although it may have a valuable role as a step toward smoking cessation.

cohort studies; harm reduction; longevity; mortality; smoking; smoking cessation

Abbreviations: CI, confidence interval; HR, hazard ratio; ICD-9, *International Classification of Diseases, Ninth Revision*; ICD-10, *International Classification of Diseases, Tenth Revision*.

Despite clear evidence that smoking cessation brings substantial health benefits and financial savings, many smokers are unable or unwilling to quit. Consequently, researchers have tried to establish whether reducing the number of cigarettes smoked could bring about sufficient long-term health benefits to be recommended as a worthwhile alternative to quitting. A large prospective cohort study in Denmark with a mean of 15 years' follow-up found no evidence that heavy smokers who reduced their daily number of cigarettes had a lower risk of death from all causes or of fatal or nonfatal myocardial infarction (1, 2). A systematic review of the health benefits of smoking reduction identified 24 other studies, most of which were small and with short follow-up (3). It concluded that a substantial reduction in smoking seemed to have a small health benefit, but more research was needed to determine the long-term effects. Two other large prospective cohort studies found that smoking reduction did not lower the risk of death from all causes (4) or the incidence of stroke or myocardial infarction (5). However, a recent cohort study of working Israeli men who were recruited in 1963, rescreened in 1965, and followed up for 32 years found that smoking reducers had significantly lower hazard ratios for mortality than did maintainers (6). The apparent benefit of reducing smoking was seen primarily in heavy smokers and for cardiovascular disease mortality. In light of these results, the authors suggested that reducing the number of cigarettes

smoked was a plausible risk-reduction strategy for heavy smokers who are unable to quit. Advocating reduction rather than cessation for some smokers would be a major shift in approach that should have solid support from several rigorous studies. In an attempt to reproduce the Israeli findings, we applied the methodology of that study to 2 comparable cohorts in Scotland that were recruited and rescreened in the 1970s and followed up until the end of 2010.

MATERIALS AND METHODS

Participants were from 2 of the Midspan prospective cohort studies, which originated in the postwar effort to control pulmonary tuberculosis by screening with mass miniature radiography (7). Recruitment for the Collaborative Study of working men ($n = 6,022$) and women ($n = 1,006$) took place between 1970 and 1973 in 27 workplaces in the central belt of Scotland (8). Recruitment for the Renfrew/Paisley Study of the general population (7,049 men and 8,353 women) took place between 1972 and 1976 in 2 Scottish towns (9). Second screenings took place in 1977 for the Collaborative Study and in 1977–1979 for the Renfrew/Paisley Study. Participants in both studies completed similar questionnaires and had similar screening examinations. The present analysis used data from men and women who were cigarette smokers at the first screening and who took part in the second screening.

The questionnaires at both screenings included questions on smoking behavior, occupation, diabetes, angina, and severe chest pain lasting for at least 30 minutes. At the first screening, blood pressure, height, and weight were measured, electrocardiography was performed, and a blood sample was taken to test for plasma cholesterol levels; these procedures were repeated at the second screening except for cholesterol measurements.

As in the Israeli study, detailed questions about smoking behavior allowed subjects to be categorized as smoking 1–10, 11–20, or ≥21 cigarettes per day at the 2 screening occasions, or as having quit smoking by the second screening (6). Smokers were defined at the second screening as having increased (moved to a higher category), maintained (stayed in the same category), or reduced (moved to a lower category) their smoking intensity or as having quit smoking. For additional analyses, the "reduced" group was subdivided into those who reduced from ≥21 cigarettes/day (heavy smokers) or from ≤20 cigarettes/day (lighter smokers).

We defined 6 social class groups based on occupation according to the General Register Office Classification of Occupations (10) ranging from I (professional) to V (unskilled), with manual social class defined as III manual (skilled manual), IV (partly skilled), and V (unskilled). Women who classified themselves as "housewives" in the Renfrew/Paisley Study were allocated the social classes of their husbands. Diabetes was self reported. Angina was defined according to the Rose questionnaire (11). At the screening examination, blood pressure was measured with participants seated. Height and weight were measured, and body mass index (weight (kg)/height $(m)^2$) was calculated. Ischemia on electrocardiogram was defined as any of the following Minnesota codes: 1.1–1.3, 4.1–4.4, 5.1–5.3, or 7.1 (12). Preexisting coronary heart disease was defined as any angina (definite or possible (13)), severe chest pain lasting at least 30 minutes, or ischemia on electrocardiogram.

Mortality follow-up was established by flagging participant data in the National Health Service Central Register. Dates and causes of death were obtained until the end of 2010. Cardiovascular disease mortality was defined as coronary heart disease (*International Classification of Diseases, Ninth Revision* (ICD-9), codes 410–414 or *International Classification of Diseases, Tenth Revision* (ICD-10), codes I20–I25) or stroke (ICD-9 codes 430–438 or ICD-10 codes I60–I69 or G45). Non–cardiovascular disease mortality was defined as all other causes of death. Lung cancer mortality was defined as ICD-9 code 162 or ICD-10 codes C33–C34. Nine Collaborative Study and 23 Renfrew/Paisley Study participants who left the United Kingdom were censored at their leaving dates.

The age range for participation in the Renfrew/Paisley Study was 45–64 years (mean = 53 years). Collaborative Study participants were included in this analysis if they were aged 40 years or older at the first screening (mean = 49 years, maximum = 65 years) to achieve a similar age range to that of participants in the Israeli study (6). After the exclusion of participants who were lost to follow-up (1 Collaborative Study and 4 Renfrew/Paisley Study participants), there were 1,524 (1,299 male and 225 female) Collaborative Study and 3,730 (1,878 male and 1,852 female) Renfrew/Paisley Study participants who were current smokers at the first screening and who took part in the second screening.

Statistical analyses were conducted by using Stata, version 11, software (StataCorp LP, College Station, Texas), and all P values were 2-sided. Means and percentages of risk factors were standardized by 5-year age groups. Tests for trends across smoking intensity categories were calculated by using regression analysis for continuous variables or logistic regression analysis for discrete variables. Cox proportional hazards regression models were used to calculate the hazard ratios of mortality for each smoking intensity category and to calculate P values for trend by using smoking intensity as a continuous variable. The proportional hazards assumption was checked by using Schoenfeld residuals. Analyses of mortality from cardiovascular disease and non–cardiovascular disease accounted for competing risks by using the stcrreg procedure in Stata, version 11, software, which uses the methodology of Fine and Gray (14). Participants who maintained their smoking intensity were considered the baseline group. The first model included adjustments for age at the second screening, social class, and number of cigarettes smoked at the first screening. The second model also adjusted for systolic blood pressure, body mass index, diabetes, and preexisting coronary heart disease at the second screening and plasma cholesterol level at first screening. The few missing variables (0.6% in the Collaborative Study and 3.2% in the Renfrew/Paisley Study) were replaced by the sex- and study-specific mean (or mode for social class). Follow-up was from the date of the second screening until the date of death, date of leaving the United Kingdom, or December 31, 2010. Interactions with sex were not significant (P for interaction for all-cause mortality was 0.15 in the Collaborative Study and 0.52 in the Renfrew/Paisley Study), so results are presented with data from men and women combined, and

analyses included a term for sex. Results for men and women are presented separately in Web Tables 1–3 available at http://aje.oxfordjournals.org/.

Logistic regression was used to calculate the odds ratios of survival by smoking intensity category to age 75 years in both studies and to age 80 years in the Renfrew/Paisley Study only (because 23 surviving Collaborative Study participants had not reached age 80 years at the end of follow-up). Tests for trend used smoking intensity as a continuous variable. Participants who had left the United Kingdom during follow-up were excluded from these analyses only, because there was no information on death status. Higher odds ratios represent better outcomes in these analyses, in contrast to hazard ratios of mortality, in which higher hazard ratios represent worse outcomes.

Finally, the 2 studies were combined and analyzed with a term for study included. There were 3 men who participated in both studies; only their Collaborative Study data were used in these joint analyses because that study was conducted first (15). Interactions with study were not significant, apart from analysis of all-cause mortality with the "reduced" category subdivided into heavy and lighter smokers (P for interaction = 0.017); therefore, these analyses were conducted separately for the 2 studies. Analyses were repeated, excluding deaths in the first 3 years to address reverse causation. Further analyses included adjustment for duration of smoking from smoking initiation to first screening, which excluded 16 Renfrew/Paisley Study participants with missing data on age at smoking initiation.

RESULTS

Smoking categories at the first and second screenings are shown in Tables 1 and 2 for the Collaborative and Renfrew/Paisley Studies, respectively. In the Collaborative Study, 13.8% of subjects increased, 59.2% maintained, and 9.6% reduced their cigarette consumption, and 17.3% quit smoking between the 2 screenings (Table 3). In the Renfrew/Paisley Study, 9.9% of subjects increased, 64.6% maintained, and 12.6% reduced their cigarette consumption, and 13.0% quit smoking. Differences in risk factors among the smoking change groups were apparent in participants who quit smoking. Quitters in the Collaborative Study had higher cholesterol levels and body mass index values, and fewer were from manual social classes. Quitters in the Renfrew/Paisley Study had higher systolic blood pressure and body mass index values.

During a median follow-up of 21.1 (maximum, 33.9) years in the Collaborative Study, 1,252 participants (82%) died. During a median follow-up of 18.7 (maximum, 33.8) years in the Renfrew/Paisley Study, 3,187 participants (85%) died. There was no evidence of lower mortality in those who reduced cigarette consumption compared with those who maintained cigarette consumption. The multivariate adjusted hazard ratios of mortality were 0.91 (95% confidence interval (CI): 0.75, 1.10) in the Collaborative Study and 1.08 (95% CI: 0.97, 1.20) in the Renfrew/Paisley Study (Table 4). Renfrew/Paisley Study participants who increased their smoking intensity had higher hazard ratios of mortality (multivariate adjusted hazard ratio (HR) = 1.17, 95% CI: 1.04, 1.32), but no significant rate was seen for increasers in the Collaborative Study. There was clear evidence of lower mortality in quitters (multivariate adjusted HRs of 0.66 (95% CI: 0.56, 0.78) and 0.75 (95% CI: 0.67, 0.84) in the Collaborative and Renfrew/Paisley Studies, respectively). Additional adjustment for smoking duration had a negligible effect; the multivariate adjusted hazard ratio for reducers was 0.92 (95% CI: 0.76, 1.11) compared with 0.91 (95% CI: 0.75, 1.10) without this adjustment for the

Table 1. Cigarette Smoking Intensity at a Second Screening (in 1977) Compared With That at a First Screening (in 1970–1973) in the Collaborative Study, Scotland

Smoking at First Screening, cigarettes/day	Smoking at Second Screening, cigarettes/day									
	0		1–10		11–20		≥21		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Men and women (n = 1,524)										
1–10	60	3.9	160	10.5	59	3.9	8	0.5	287	18.8
11–20	140	9.2	85	5.6	526	34.5	144	9.4	895	58.7
≥21	64	4.2	4	0.3	58	3.8	216	14.2	342	22.4
Total	264	17.3	249	16.3	643	42.2	368	24.1	1,524	100
Men (n = 1,299)										
1–10	57	4.4	133	10.2	43	3.3	6	0.5	239	18.4
11–20	129	9.9	70	5.4	431	33.2	125	9.6	755	58.1
≥21	64	4.9	4	0.3	52	4.0	185	14.2	305	23.5
Total	250	19.2	207	15.9	526	40.5	316	24.3	1,299	100
Women (n = 225)										
1–10	3	1.3	27	12.0	16	7.1	2	0.9	48	21.3
11–20	11	4.9	15	6.7	95	42.2	19	8.4	140	62.2
≥21	0	0	0	0	6	2.7	31	13.8	37	16.4
Total	14	6.2	42	18.7	117	52.0	52	23.1	225	100

Table 2. Cigarette Smoking Intensity at a Second Screening (in 1977–1979) Compared With That at a First Screening (in 1972–1976) in the Renfrew/Paisley Study, Scotland

Smoking at First Screening, cigarettes/day	Smoking at Second Screening, cigarettes/day									
	0		1–10		11–20		≥21		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Men and women (n = 3,730)										
1–10	166	4.5	483	12.9	169	4.5	9	0.2	827	22.2
11–20	213	5.7	272	7.3	1,521	40.8	190	5.1	2,196	58.9
≥21	105	2.8	6	0.2	191	5.1	405	10.9	707	19.0
Total	484	13.0	761	20.4	1,881	50.4	604	16.2	3,730	100
Men (n = 1,878)										
1–10	53	2.8	133	7.1	71	3.8	7	0.4	264	14.1
11–20	141	7.5	102	5.4	690	36.7	122	6.5	1,055	56.2
≥21	91	4.8	5	0.3	135	7.2	328	17.5	559	29.8
Total	285	15.2	240	12.8	896	47.7	457	24.3	1,878	100
Women (n = 1,852)										
1–10	113	6.1	350	18.9	98	5.3	2	0.1	563	30.4
11–20	72	3.9	170	9.2	831	44.9	68	3.7	1,141	61.6
≥21	14	0.8	1	0.1	56	3.0	77	4.2	148	8.0
Total	199	10.7	521	28.1	985	53.2	147	7.9	1,852	100

Collaborative Study and 1.07 (95% CI: 0.96, 1.19) compared with 1.07 (95% CI: 0.97, 1.19) for the Renfrew/Paisley Study (excluding 16 subjects with missing data).

We analyzed heavy smokers (≥21 cigarettes/day) who reduced smoking intensity separately from lighter smokers (≤20 cigarettes/day) who reduced smoking intensity and obtained contrasting results. In the Collaborative Study, there was a significantly lower multivariate adjusted hazard ratio of mortality for the heavy smokers who reduced smoking intensity (HR = 0.67, 95% CI: 0.50, 0.90), which was similar to that for quitters. The lighter smokers who reduced smoking intensity had a nonsignificant hazard ratio of 1.17 (95% CI: 0.92, 1.48). In the Renfrew/Paisley Study, there was no suggestion of lower mortality for smoking reduction among either heavy smokers (HR = 1.14, 95% CI: 0.97, 1.33) or lighter smokers (HR = 1.04, 95% CI: 0.91, 1.19) (data not shown).

Hazard ratios of cardiovascular disease mortality that used competing risk models were no different across the smoking intensity categories in either cohort (Table 4). There was lower mortality from non–cardiovascular disease causes among quitters in both cohorts but not among reducers when using competing risk models. In the combined studies, there was lower mortality from lung cancer among quitters (multivariate adjusted HR = 0.53, 95% CI: 0.39, 0.71) but not among reducers (multivariate adjusted HR = 0.91, 95% CI: 0.70, 1.19) (data not shown). The overall results were similar for men and women separately (Web Table 1). Results were also similar when both cohorts were combined (Table 5 for men and women, Web Table 2 for men and women separately). The exclusion of deaths in the first 3 years had essentially no effect on the results (data not shown).

The multivariate odds ratios of surviving to age 75 years were no higher in reducers than in maintainers in both studies. The odds ratios were 1.07 (95% CI: 0.74, 1.54) in the Collaborative Study and 0.87 (95% CI: 0.7, 1.07) in the Renfrew/Paisley Study (Table 6). The multivariate adjusted odds of surviving to age 75 years were lower for Collaborative Study participants who increased their smoking. Collaborative and Renfrew/Paisley Study participants who quit smoking had higher odds of surviving to age 75 years. Combining the 2 cohorts produced similar results. Survival to age 80 years was higher among Renfrew/Paisley Study participants who quit smoking (odds ratio = 1.64, 95% CI: 1.33, 2.02). Results for men and women are shown separately in Web Table 3.

DISCUSSION

In this long-term prospective study of both working and general population cohorts, we were unable to detect a significant overall long-term survival benefit among smokers who reported reducing their daily consumption of cigarettes between 2 screenings a few years apart. Our results can be usefully compared with those of a recently published Israeli study of comparable size, methodology, and duration of follow-up, which found lower long-term all-cause and cardiovascular disease mortality rates among smoking reducers (6). Two other large cohort studies found that smoking reduction did not reduce the risk of dying (4) or of experiencing a stroke or myocardial infarction (5). A third large cohort study found that hazard ratios of all causes of death and fatal or nonfatal myocardial infarction were not reduced after 15.5 years of follow-up (1, 2). The main features and outcomes of the 6 cohort studies are summarized in Table 7. All studies used essentially the same methods of 2 screenings a few years apart and subsequent follow-up. Five used death

Table 3. Risk Factors[a] According to Changes in Smoking Intensity Between 2 Screenings of the Collaborative (in 1970–1973 and 1977) and Renfrew/Paisley (in 1972–1976 and 1977–1979) Studies, Scotland

Smoking Intensity Changes by Cohort	Total		Age, years[b]		Systolic Blood Pressure, mm Hg[b]		Cholesterol, mmol/L[c]		Body Mass Index[b,d]		Preexisting Coronary Heart Disease[b]		Manual Social Class[c]	
	No.	%	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	%	95% CI	%	95% CI
Collaborative Study Cohort														
Increased	211	13.8	52.9	52.3, 53.6	142.4	139.6, 145.2	5.75	5.60, 5.89	24.9	24.5, 25.2	23.4	17.8, 29.1	61.5	54.8, 68.2
Maintained	902	59.2	54.2	53.8, 54.5	142.4	141.1, 143.7	5.67	5.60, 5.73	24.5	24.3, 24.7	22.5	19.7, 25.2	68.0	64.9, 71.0
Reduced	147	9.6	55.3	54.5, 56.0	145.7	142.0, 149.4	5.77	5.59, 5.95	25.1	24.6, 25.6	27.5	20.2, 34.8	73.2	65.8, 80.7
Quit	264	17.3	53.7	53.1, 54.3	145.3	142.9, 147.7	5.86	5.73, 5.99	26.1	25.7, 26.4	26.0	20.8, 31.1	58.5	52.6, 64.4
P_{trend}			0.16		0.037		0.045		<0.0001		0.12		0.26	
Renfrew/Paisley Study Cohort														
Increased	368	9.9	56.5	56.0, 57.1	144.2	142.0, 146.5	6.05	5.92, 6.17	24.5	24.1, 24.9	31.0	26.2, 35.7	67.8	62.8, 72.7
Maintained	2,409	64.6	57.5	57.3, 57.7	145.4	144.6, 146.2	6.13	6.08, 6.17	24.6	24.4, 24.7	30.2	28.4, 32.0	61.2	59.2, 63.2
Reduced	469	12.6	58.8	58.3, 59.3	143.6	141.6, 145.5	6.10	6.01, 6.20	24.5	24.2, 24.9	33.1	28.8, 37.4	64.7	60.2, 69.2
Quit	484	13.0	59.0	58.5, 59.5	149.6	147.8, 151.5	6.07	5.98, 6.16	26.2	25.9, 26.6	33.2	28.9, 37.5	59.4	55.0, 63.9
P_{trend}			<0.0001		0.003		0.72		<0.0001		0.20		0.12	

Abbreviation: CI, confidence interval.

[a] Adjusted for age at the second screening (except mean age).

[b] Measured at second screening.

[c] Measured at first screening.

[d] Body mass index is weight (kg)/height $(m)^2$.

Table 4. Hazard Ratios of All-Cause, Cardiovascular Disease, and Non–Cardiovascular Disease Mortality According to Changes in Smoking Intensity Between 2 Screenings of the Collaborative (in 1970–1973 and 1977) and Renfrew/Paisley (in 1972–1976 and 1977–1979) Studies, Scotland

Smoking Intensity Changes by Cohort	Total			All-Cause Mortality						Cardiovascular Disease Mortality[a]						Non–Cardiovascular Disease Mortality[a]					
	No.	%	Person-Years	No. of Deaths	Rate[b]	HR[c]	95% CI	HR[d]	95% CI	No. of Deaths	Rate[b]	HR[c]	95% CI	HR[d]	95% CI	No. of Deaths	Rate[b]	HR[c]	95% CI	HR[d]	95% CI
Collaborative Study Cohort																					
Increased	211	13.8	4,215	172	408.0	1.14	0.96, 1.35	1.15	0.97, 1.35	67	159.0	1.02	0.78, 1.34	0.99	0.75, 1.30	105	249.1	1.11	0.89, 1.38	1.12	0.90, 1.39
Maintained	902	59.2	18,538	765	412.7	1	Referent	1	Referent	301	162.4	1	Referent	1	Referent	464	250.3	1	Referent	1	Referent
Reduced	147	9.6	2,849	128	449.2	0.96	0.79, 1.16	0.91	0.75, 1.10	52	182.5	1.01	0.74, 1.36	0.90	0.66, 1.22	76	266.7	0.97	0.76, 1.24	1.0	0.78, 1.28
Quit	264	17.3	6,092	187	307.0	0.69	0.59, 0.81	0.66	0.56, 0.78	83	136.3	0.93	0.73, 1.19	0.84	0.66, 1.08	104	170.7	0.71	0.57, 0.88	0.74	0.59, 0.92
P_{trend}							<0.0001		<0.0001				0.56		0.19				0.001		0.003
Renfrew/Paisley Study Cohort																					
Increased	368	9.9	7,010	320	456.5	1.16	1.03, 1.31	1.17	1.04, 1.32	120	171.2	1.02	0.83, 1.24	1.03	0.84, 1.26	200	285.3	1.10	0.95, 1.29	1.10	0.95, 1.29
Maintained	2,409	64.6	45,596	2,050	449.6	1	Referent	1	Referent	771	169.1	1	Referent	1	Referent	1,279	280.5	1	Referent	1	Referent
Reduced	469	12.6	8,021	425	529.9	1.10	0.99, 1.22	1.08	0.97, 1.20	173	215.7	1.11	0.94, 1.32	1.14	0.95, 1.35	252	314.2	0.97	0.84, 1.12	0.97	0.84, 1.12
Quit	484	13.0	9,424	392	416.0	0.77	0.69, 0.86	0.75	0.67, 0.84	179	189.9	1.11	0.94, 1.31	1.05	0.88, 1.24	213	226.0	0.72	0.62, 0.83	0.73	0.63, 0.85
P_{trend}							<0.0001		<0.0001				0.18		0.46				<0.0001		<0.0001

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Determined by using competing risk models.

[b] Per 10,000 person-years.

[c] Adjusted for sex, social class, and cigarettes smoked at first screening and age at second screening.

[d] Adjusted for sex, social class, cigarettes smoked, and plasma cholesterol level at first screening and age, systolic blood pressure, body mass index (weight (kg)/height $(m)^2$), diabetes, and preexisting coronary heart disease at second screening.

Table 5. Hazard Ratios of All-Cause, Cardiovascular Disease, and Non–Cardiovascular Disease Mortality According to Changes in Smoking Intensity Between 2 Screenings of the Collaborative (in 1970–1973 and 1977) and Renfrew/Paisley (in 1972–1976 and 1977–1979) Studies Combined, Scotland

Smoking Intensity Changes	Total			All-Cause Mortality					Cardiovascular Disease Mortality[a]					Non–Cardiovascular Disease Mortality[a]				
	No.	%	Person-Years	No. of Deaths	Rate[b]	HR[c]	95% CI	HR[d]	95% CI	No. of Deaths	Rate[b]	HR[c]	95% CI	HR[d]	95% CI	No. of Deaths	Rate[b]	HR[c]	95% CI	HR[d]	95% CI
Increased	579	11.0	11,225	492	438.3	1.16	1.05, 1.28	1.16	1.06, 1.28	187	166.6	1.02	0.87, 1.20	1.02	0.87, 1.20	305	271.7	1.11	0.98, 1.25	1.11	0.98, 1.25
Maintained	3,309	63.0	64,082	2,813	439.0	1	Referent	1	Referent	1,071	167.1	1	Referent	1	Referent	1,742	271.8	1	Referent	1	Referent
Reduced	616	11.7	10,871	553	508.7	1.06	0.97, 1.16	1.04	0.95, 1.14	225	207.0	1.08	0.93, 1.26	1.08	0.93, 1.25	328	301.7	0.97	0.86, 1.10	0.97	0.86, 1.10
Quit	747	14.2	15,485	579	373.9	0.74	0.68, 0.81	0.72	0.66, 0.79	262	169.2	1.06	0.92, 1.21	0.98	0.85, 1.13	317	204.7	0.71	0.63, 0.80	0.73	0.64, 0.82
P_{trend}				<0.0001				<0.0001					0.41		0.94				<0.0001		<0.0001

Abbreviations: CI, confidence interval; HR, hazard ratios.

[a] Determined by using competing risk models.

[b] Per 10,000 person-years.

[c] Adjusted for sex, social class, study, and cigarettes smoked at the first screening and age at the second screening.

[d] Adjusted for sex, social class, study, cigarettes smoked, and plasma cholesterol level at the first screening and age, systolic blood pressure, body mass index (weight (kg)/height (m)^2), diabetes, and preexisting coronary heart disease at the second screening.

as the main outcome measure, and 1 used the incidence of stroke or myocardial infarction. There were clear differences in the size and composition of the cohorts and in the duration of follow-up. Four studies used the same definitions of smoking groups and smoking reduction, and 2 studies used different definitions. Although the Scottish and Israeli cohorts were the most similar in terms of size, screening intervals, and duration of follow-up, the apparent overall lack of benefit from smoking reduction for all-cause mortality found in the Scottish analysis concurred with Norwegian (4), Danish (1), and Korean (5) studies. However, the contrast is not as clear as it might first appear. In the Collaborative Study but not the Renfrew/Paisley Study, heavy smokers who reduced their smoking intensity had a significantly lower mortality rate than either smokers who maintained their cigarette consumption or, surprisingly, light smokers who reduced their consumption. This is similar to the findings in the Israeli cohort, in which a significant reduction in mortality risk was found among heavy smokers but not among light smokers who reduced their smoking intensity (6). Furthermore, although the analysis of the combined Danish cohorts did not show a benefit from reducing smoking after 15.5 years of follow-up, the risk of lung cancer among reducers was significantly lower after 18 years of follow-up (HR = 0.73, 95% CI: 0.54, 0.98) (16). However, we did not find that mortality from lung cancer was lower among those who reduced their smoking when we combined the data from our 2 cohorts.

Given the abundant evidence for a dose-response relationship between the lifetime number of cigarettes smoked and subsequent morbidity and mortality, it would seem logical to expect that reducing the number of cigarettes smoked would lead to a lower mortality rate. The authors of the Israeli study suggested the different results could be caused by insufficient length of follow-up of the cohorts in the previously reported studies. This is given some support by the finding of reduced lung cancer risk in the Danish pooled cohorts after a longer period of follow-up (16). However, with more than 30 years of follow-up, during which time more than 80% of the participants died, the Scottish cohort studies still did not show unequivocal benefit. The Scottish cohort studies had the added benefits of including both general and working populations of men and women, whereas the Israeli study included only working men. Some explanation may lie in the contrasting patterns of smoking reduction in the various studies. The Israeli study showed that the main health benefit appeared to be among heavy smokers who reduced their smoking, a finding mirrored in the Collaborative Study cohort but not the Renfrew/Paisley Study cohort. A notable feature of the Israeli cohort was the relatively high proportion of subjects who were heavy smokers and who reduced the number of cigarettes they smoked between the first and second screenings. This proportion represented 13.4% of the Israeli cohort compared with 4.1% and 5.3% of the Collaborative Study and Renfrew/Paisley Study cohorts, respectively, and 6.7% of the much larger Korean cohort (5). This may, at least in part, explain the observed differences in overall outcomes.

Crucially, all 6 cohorts lacked information about smoking behavior and the reasons for any changes in smoking during the follow-up period. Therefore, there is uncertainty about the proportions of "reducers" in each cohort who sustained their

Table 6. Odds Ratios of Surviving to Age 75 or 80 Years According to Changes in Smoking Intensity Between 2 Screenings of the Collaborative (in 1970–1973 and 1977) and Renfrew/Paisley (in 1972–1976 and 1977–1979) Studies, Scotland

Smoking Intensity Changes by Cohort	Total No.[a]	Survival to Age 75 Years						Survival to Age 80 Years					
		No.	%	OR[b]	95% CI	OR[c]	95% CI	No.	%	OR[b]	95% CI	OR[c]	95% CI
Collaborative Study Cohort													
Increased	207	97	46.9	0.69	0.50, 0.94	0.69	0.50, 0.94						
Maintained	900	488	54.2	1	Referent	1	Referent						
Reduced	146	77	52.7	1.0	0.70, 1.43	1.07	0.74, 1.54						
Quit	262	172	65.6	1.68	1.25, 2.25	1.76	1.30, 2.38						
P_{trend}					<0.0001		<0.0001						
Renfrew/Paisley Study Cohort													
Increased	367	212	57.8	0.89	0.71, 1.12	0.88	0.69, 1.11	136	37.1	0.82	0.65, 1.03	0.80	0.63, 1.01
Maintained	2,393	1,455	60.8	1	Referent	1	Referent	987	41.2	1	Referent	1	Referent
Reduced	467	264	56.5	0.88	0.71, 1.08	0.87	0.70, 1.07	165	35.3	0.85	0.69, 1.05	0.83	0.67, 1.03
Quit	480	324	67.5	1.37	1.11, 1.70	1.44	1.16, 1.80	247	51.5	1.57	1.28, 1.92	1.64	1.33, 2.02
P_{trend}					0.012		0.005				<0.0001		<0.0001
Collaborative and Renfrew/Paisley Cohorts Combined[d]													
Increased	574	309	53.8	0.81	0.67, 0.98	0.81	0.67, 0.97						
Maintained	3,291	1,941	59.0	1	Referent	1	Referent						
Reduced	613	341	55.6	0.91	0.76, 1.09	0.92	0.76, 1.10						
Quit	741	495	66.8	1.49	1.25, 1.77	1.57	1.31, 1.87						
P_{trend}					<0.0001		<0.0001						

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] Excludes 32 subjects who left the United Kingdom during the follow-up period (9 in the Collaborative cohort and 23 in the Renfrew/Paisley cohort).

[b] Adjusted for sex, social class, and cigarettes smoked at the first screening and age at the second screening.

[c] Adjusted for sex, social class, cigarettes smoked, and plasma cholesterol level at the first screening and age, systolic blood pressure, body mass index (weight (kg)/height $(m)^2$), diabetes, and preexisting coronary heart disease at the second screening.

[d] Odds ratios are also adjusted for study.

reported levels of reduction, subsequently quit smoking, or resumed heavier smoking. A third screening, several years after the second, was carried out on about half of the "reducers" in the Danish cohort (2). In this third screening, approximately 50% of subjects had continued to smoke at a reduced level, 25% had quit smoking, and 25% had resumed heavy smoking.

We also know little about the behavior during follow-up of the "maintainers," with whom the "reducers" are compared. All of the cohorts had substantial numbers of smokers who increased their daily cigarette consumption between the 2 screenings, emphasizing the wide variation and unpredictability of smoking behavior. Given the changes in smoking status observed in all cohorts between the first and second screenings, it is inevitable that many of the "maintainers" will have changed their cigarette consumption or will have quit smoking during the years of follow-up. Consequently, the baseline against which the "reducers" are compared is itself subject to considerable uncertainty and could vary between the cohorts.

In a systematic review of the health benefits of smoking reduction, Pisinger and Godtfredsen (3) found that most of the 25 studies meeting their criteria were small, with short follow-up. They focused mainly on biological markers of smoking intensity, cardiovascular risk factors, or intermediate outcomes such as the level of asthma control, the birth weights of the babies of pregnant smokers, or hospital admissions for chronic obstructive pulmonary disease. In small controlled studies, many smokers were unable to sustain reduced smoking levels. The reduction in biochemical markers of smoking in these studies was, on average, less than would be expected, indicating that some smokers may have compensated for the reduced number of cigarettes by puffing more frequently or more intensely or by smoking more of each cigarette (17–19). Studies in the review that included smokers who had significantly reduced their smoking (often defined as a >50% reduction in baseline smoking) found an improvement in respiratory symptoms and some cardiovascular risk factors. However, the benefits of less substantial smoking reduction were much less clear (3).

Smoking reduction in itself, therefore, may not result in health improvement; however, there is increasing evidence

Table 7. Main Features of Prospective Cohort Studies Assessing the Long-Term Impact of Smoking Reduction

First Author, Year (Reference No.)	Participants, Country	Age at Baseline, years	No. of Smokers in Cohort	Categories of Smoking Intensity, cigarettes/day	Definition of Smoking Reducer	First Year Screened	Years to Second Screening	No. of Reducers	Years of Follow-Up	RR of Death of Reducers Versus Maintainers[a]	95% CI
Gerber, 2012 (6)	Male civil servants and municipal workers, Israel	≥40	4,633	1–10, 11–20, and ≥21	Move to lower group	1963	2	787	32	0.85	0.77, 0.95
Current paper	Working men and women, Scotland	40–65	1,524	1–10, 11–20, and ≥21	Move to lower group	1970–1973	3–6	147	33	0.91	0.75, 1.10
Current paper	Community sample of men and women, Scotland	45–64	3,730	1–10, 11–20, and ≥21	Move to lower group	1972–1976	2–6	469	31–33	1.08	0.97, 1.20
Godtfredsen, 2002 (1)	Pooled community and occupational samples, men and women, Denmark	20–93	12,880	1–14 and ≥15	>50% Reduction from ≥15/day	1967–1981	5–10	858	15.5 (mean)	1.02[b]	0.89, 1.17
Tverdal, 2006 (4)	Community sample men and women, Norway	20–49	23,743	1–14 and ≥15	>50% Reduction from ≥15/day	1974–1978	3–13	475	21.2 (mean)	1.02[b]	0.84, 1.22
Song, 2008 (5)	Male civil servants, Korea	30–58	300,767	1–9, 10–19, and ≥20	Move to lower group	1990	2	39,045	9	Nonsignificant reductions in RR of stroke or myocardial infarction[b]	

Abbreviations: CI, confidence interval; RR, relative risk.

[a] All-cause mortality unless specified.

[b] Compared with heavy smokers who maintained the same smoking intensity.

that it has a potentially important role as a step toward smoking cessation. Smokers who are reducing their cigarette smoking are more likely to report that they intend to quit, want to quit, and are confident in their ability to quit (20, 21). There is also good evidence that reducing smoking before quitting with the aid of nicotine replacement therapy is just as effective as abrupt cessation, and that the use of nicotine replacement therapy when reducing smoking can increase the rate at which smokers try and succeed in quitting (22). Nicotine replacement therapy was not available when participants in the studies considered here reduced their smoking.

In conclusion, the long-term follow-up of these 2 Scottish cohorts does not provide sufficient evidence of benefit to endorse the Israeli conclusion that "reducing smoking intensity may be advised for heavy smokers who cannot quit abruptly" (6, p. 1011). Existing research does not provide useful guidance for the level of reduction of cigarette consumption required to confer meaningful health benefits. On the other hand, continued smoking, even at low levels, clearly carries substantially increased health risks (23). Reducing the frequency of smoking should thus primarily be recommended as a short-term step toward cessation.

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